# Qualitative optical-thermal model of argon, selective, and microsecond infrared laser trabeculoplasty

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## ABSTRACT

**Purpose.** The purpose of this work was to develop a model to predict and compare laser-trabecular meshwork interactions during laser trabeculoplasty with three different lasers. **Methods.** A qualitative multilayer optical-thermal model of the trabecular meshwork was developed. The model was used to estimate the penetration depth and heat diffusion volume during laser trabeculoplasty with a continuous wave argon laser (ALT), a Q-switched frequency-doubled Nd:YAG laser (SLT), and a flashlamp-pumped near-infrared alexandrite or titanium sapphire laser emitting microsecond pulses (μs-IRLT). **Results.** The model predicts that both SLT and μs-IRLT produce selective heating of pigmented trabecular meshwork cells with negligible heat diffusion to surrounding structures and with a deeper penetration at the infrared wavelength. A preliminary quantitative analysis indicates that selective targeting of spherical pigments is achieved as long as the pulse duration remains less than approximately 1μs. **Conclusion.** The qualitative model indicates that infrared laser trabeculoplasty with microsecond pulses can produce selective targeting of pigmented trabecular meshwork cells with a deeper penetration than SLT.

**Keywords:** trabeculoplasty, laser, glaucoma, thermal, heating, trabecular meshwork

## 1. INTRODUCTION

Laser trabeculoplasty (LT) is a treatment for primary open-angle glaucoma whereby a laser beam is focused onto equally-spaced spots applied in a ring pattern on the trabecular meshwork (TM)[1,2,3]. In the standard LT procedure, which uses an argon laser beam (ALT) emitting 0.1W at 514 nm for 0.1s, the beam is delivered through a gonioscopic lens placed in contact with the cornea to produce a focused spot diameter on the order of 50 μm[1,2,3]. The goal of ALT is to produce a thermal coagulation of the TM at each treatment spot. In clinical practice, the laser power is adjusted until it is below the threshold for bubble formation by using practice shots on the TM[2,3]. ALT produces a combination of thermally-induced TM cell damage and cell death and local thermal contraction of the TM. Together, these effects lead to an increase in aqueous outflow following the treatment. ALT was found to successfully reduce or control intraocular pressure (IOP) in approximately 80% of patients, but the effect diminishes with time[2,3]. Re-treatment is not possible due to the extensive irreversible TM damage produced by the initial treatment.

Even though ALT is a successful procedure, a number of alternate laser sources have been investigated for LT, in an attempt to minimize collateral thermal damage and allow re-treatments. Clinical studies have shown that using a continuous-wave near-infrared diode laser emitting at 810 nm, which penetrates deeper in the TM than the argon laser, did not provide any clinical advantage over standard ALT[3]. On the other hand, recent experimental studies demonstrated the feasibility of selectively targeting pigmented TM cells in culture using a frequency-doubled Q-switched Nd:YAG laser emitting nanosecond pulses at 532 nm[4]. These experiments led to the development of

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Selective Laser Trabeculoplasty (SLT), a new technique for LT where a Q-switched frequency-doubled Nd:YAG laser beam with a pulse duration on the order of 3 ns and an energy per pulse on the order of 1 mJ is focused onto a 400 μm diameter spot on the TM[5]. Selective absorption of the laser radiation by the pigments in TM cells leads to a temperature increase of the pigment, but the pulse duration is too short to allow diffusion of heat to surrounding structures. In clinical application of SLT, no shrinkage or whitening of the TM can be seen[5]. Ultrastructural studies using electron microscopy on human cadaver eyes show minimal disruption of the TM following SLT[6]. Clinical studies demonstrate that SLT successfully reduces IOP in patients with primary open-angle glaucoma[5,7,8]. On the other hand, preliminary clinical studies have shown that a titanium-sapphire laser emitting microsecond pulses at 800 nm (μs-IRLT) can also produce increased outflow while minimizing collateral damage to the TM[9]. Compared to SLT, μs-IRLT potentially has the advantage of reaching deeper layers of the trabecular meshwork.

In order to better understand and compare the effects of different laser parameters (wavelength, pulse duration, energy, spot size) on the outcome of LT, the first step is to develop an optical thermal model of the TM during laser irradiation. Ideally, the model should provide reliable estimates of the irradiation and temperature distribution in the TM during LT to help predict the primary tissue interaction and the resulting tissue response. An accurate knowledge of the optical and thermal properties, of the beam geometry and of the anatomy of the TM is required in order to develop a reliable quantitative model for LT. To the best of our knowledge, there is only one study of the optical properties of the TM, by Farrar, Roberts *et al*, who used homogenized TM tissue[10]. Unfortunately, the TM is inhomogeneous: absorption in the TM is mainly due to intracellular melanin pigments. A homogeneous model of the TM might be useful in predicting the effect of LT with continuous wave lasers (ALT or CW diode laser LT) but it can not be used to model SLT or μs-IRLT which selectively target microstructures in the TM (pigment granules). Another roadblock when developing a quantitative optical-thermal model of LT, is that the exact composition, optical properties and concentration of the pigments vary between individuals and are unknown.

In the following, we present a preliminary qualitative optical thermal model of the TM and use the model to predict and compare the relative effects of ALT, SLT and μs-IRLT.

## 2. OPTICAL-THERMAL MODEL OF LASER TRABECULOPLASTY

### 2.1. Multilayer optical model of the trabecular meshwork

A simplified one-dimensional multilayer optical model of the trabecular meshwork (TM) was developed based on the general anatomy of the TM (Figure 1). The human TM is a 300 μm wide and 75 μm thick multilayer structure located in the anterior chamber angle between the cornea and the root of the iris[11]. It consists of sheets of trabecular beams that form a multilayer mesh. The TM serves as a filter that regulates the outflow of aqueous from the anterior chamber into Schlemm's canal. Individual TM beams are made of collagen, elastic tissue and other extracellular matrix components. The TM also contains pigmented cells that are wrapped around the trabecular beams. The trabecular sheets are separated by intertrabecular spaces filled with aqueous. The distance between trabecular sheets progressively decreases from the anterior chamber to Schlemm's canal.

The simplified optical model assumes that the TM consists of successive layers of water, collagen and extracellular matrix, and pigments arranged as shown in Figure 1. The water layers model the intertrabecular spaces filled with aqueous. The matrix layers model the trabecular beams. Pigment layers surround the matrix layers and model the pigmented cells wrapped around the trabecular beams. The model assumes that absorption of laser radiation in the matrix and water layers is negligible compared to absorption in the pigment layers. In first approximation, the pigment layers are assumed to consist of a homogeneous solution of melanin pigments in water with a concentration of 1% per volume (based on TM histology[11]).

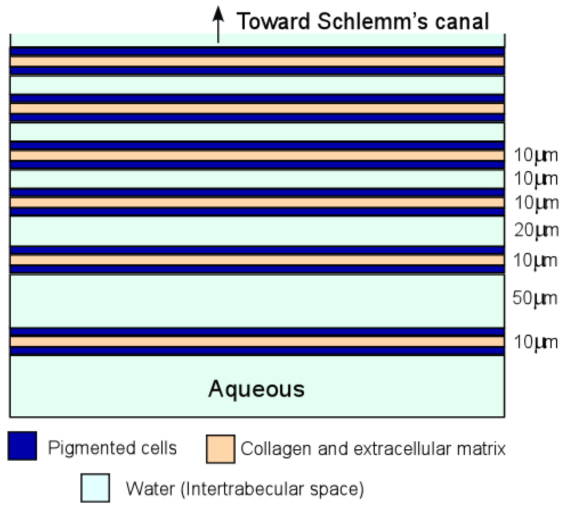


**Figure 1:** Simplified one-dimensional multilayer optical model of the trabecular meshwork

| Wavelength (nm) | Absorption Coefficient ($cm^{-1}$ / %) | Penetration Depth (µm) |
|---|---|---|
| 514 | 245 | 41 |
| 532 | 220 | 45 |
| 633 | 127 | 78 |
| 800 | 50 | 200 |

**Table 1:** Estimated absorption coefficient and penetration depth in melanin solution as a function of concentration. Pigment layers of the optical model were assumed to be homogeneous layers of 1% melanin solution in water.

### 2.2. Qualitative optical-thermal model of laser trabeculoplasty

The effect of laser trabeculoplasty (LT) was predicted by estimating the penetration depth and heat diffusion length in the trabecular meshwork (TM) during laser irradiation. Together, the penetration depth and heat diffusion length provide an estimate of the volume of heated tissue. The model does not take into account the effect of scattering. The penetration depth was calculated by combining the relative absorption spectrum of Dopa-melanin measured by Anderson and Parrish[12] with the absorption coefficient of melanin in solution measured by Vitkin *et al* at 633 nm as a function of concentration[13]. (Table 1). The diffusion length, $L_D$, was calculated by using the thermal properties of water, which yields:

$$L_D = 2 \cdot \sqrt{\chi \cdot t} = 938 \cdot \sqrt{t} \ \ \mu\text{m}.s^{-1} \quad \text{(Eq. 1)}$$

where $t$ is time in seconds and $\chi$ is the thermal diffusivity of tissue ($\chi$=2.2x$10^{-3}$ $cm^2.s^{-1}$).

## 3. RESULTS

The estimated penetration depth and heat diffusion length during ALT, SLT and µs-IRLT are listed in Table 2. During ALT, the heat diffusion length significantly exceeds the penetration depth of the laser, which indicates that the effect is caused mainly by diffusion of heat from the initial absorption volume during irradiation. The heat diffusion length during ALT exceeds the thickness of the TM. On the other hand, both SLT and µs-IRLT produce selective effects, where the heat remains localized in the initial absorption volume. Due to deeper penetration of the near-IR radiation, the model predicts that µs-IRLT reaches pigmented cells located deeper within the TM (Figure 3).

## 4. DISCUSSION

A preliminary qualitative optical-thermal model of laser trabeculoplasty (LT) was developed by combining a simplified one-dimensional multilayer optical model of the trabecular meshwork with values of the optical properties of melanin and of the heat diffusion length in water. The model was used to predict the relative heated volume during LT with three different sets of laser parameters. The model indicates that both SLT and µs-IRLT selectively target pigmented cells in the TM and that the µs-IRLT produces a deeper effect than SLT.

This first-order model relies on several limiting assumptions on the optical and thermal properties, on the structure, and on the concentration of pigments in the TM. Unfortunately, to the best of our knowledge, these parameters have not yet been accurately quantified. Any model of LT must therefore rely on numerical estimates based on anatomical data. The model also does not take into account scattering in the TM, which reduces the effective penetration of laser radiation and homogenizes the light distribution. Since scattering in biological tissue decreases as the wavelength increases we expect that scattering will further increase the difference in penetration between the µs-IRLT and ALT or SLT, since the green lasers will be scattered more strongly.

The model assumes that the TM is a multilayer structure consisting of optically homogeneous layers. The homogeneous layer model is valid only as long as both the heat diffusion length and penetration depth are much larger than the pigment diameter and separation (~1µm). When this condition is satisfied, pigments from the same layer can be lumped together and can be modeled by a homogeneous layer which has the same properties as a homogeneous solution of pigments with a concentration equal to the average concentration in the pigmented layer. The values of Table 2 demonstrate that this assumption is clearly not valid for µs-IRLT and SLT because the heat diffusion length is smaller or on the order of the pigment diameter. The homogeneous layer model therefore breaks down and an optical-thermal model at the microscopic level must be used to be able to compare the selectiveness and laser-tissue interaction during µs-IRLT and SLT. For instance, Thompson *et al*[14] developed a model to calculate the temperature in isolated spherical melanin pigment granules. The model was used by Brinkman *et al*[15] to calculate the temperature in the retinal pigment epithelium during selective photocoagulation. A preliminary quantitative calculation using a similar model indicates that heat diffusion around a 1µm diameter pigment is negligible as long as the pulse duration is less than approximately 1µs (Figure 4).

One of the main limitations of the qualitative model is that it assumes that the laser-TM interaction during LT is purely thermal. The quantitative model (Figure 4) predicts that heat remains localized in the pigments during both SLT and µs-IRLT, which implies that little or no damage is expected outside the cell containing the pigment. In reality however, the rapid temperature increase (on a nanosecond time scale) from the initial value to temperatures exceeding 200$^o$C will induce a high amplitude thermoacoustic wave that will most likely produce photomechanical damage reaching beyond the cell containing the absorbing pigment. The primary damage mechanism producing the tissue response following SLT or µs-IRLT is most likely photomechanical rather than photothermal.

| LT mode | Wavelength | Pulse duration | Penetration depth | Heat diffusion length |
|---|---|---|---|---|
| ALT | 514 nm | 100 ms | 41 µm | 300 µm |
| SLT | 532 nm | 3 ns | 46 µm | 0.05 µm |
| µs-IRLT | 800 nm | 0.2-1.0 µs | 200 µm | 0.4-0.9 µm |

**Table 2:** Estimated penetration depth and heat diffusion length during ALT, SLT and µs-IRLT.

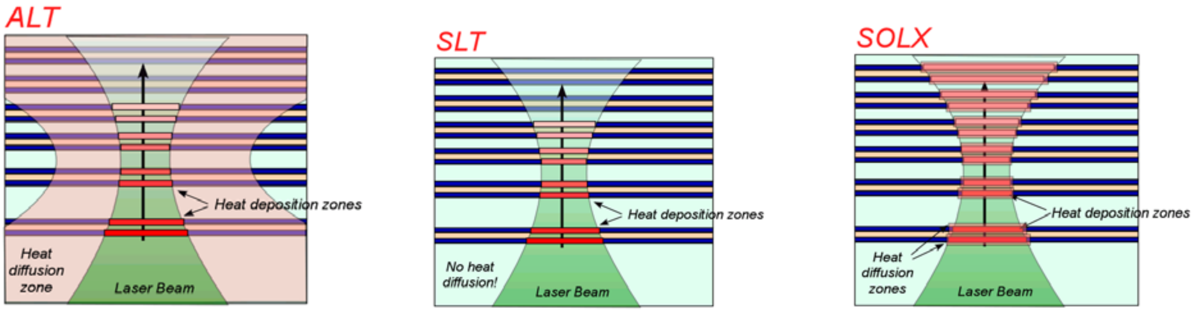


**Figure 3:** Comparison of the effects of ALT, SLT and μs-IRLT.
(Scattering is not taken into account)

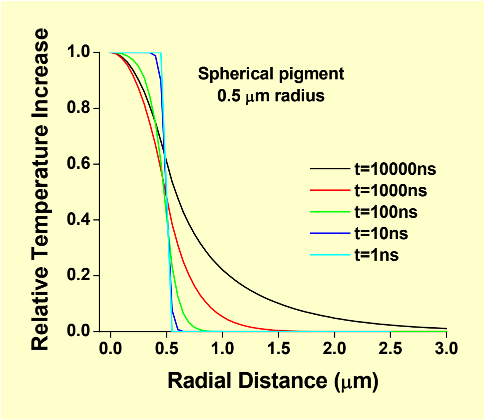


**Figure 4:** Relative temperature distribution within and surrounding an isolated 1 μm diameter spherical homogeneous melanin granule as a function of pulse duration. With clinical parameters, the temperature at the center of the pigment reaches above 200$^{o}$C.

## 5. CONCLUSIONS

A qualitative model of laser trabeculoplasty was developed to help predict and compare laser-trabecular meshwork interactions during laser trabeculoplasty with different laser parameters. The model predicts that selective targeting of the pigmented cells of the trabecular meshwork with minimal damage to surrounding trabecular beams can be achieved both with a frequency-doubled Q-switched Nd:YAG laser (SLT) and with a microsecond pulsed near-infrared laser (μs-IRLT). The model also predicts that μs-IRLT reaches deeper trabecular meshwork cells than SLT. Further studies on the optical, thermal and anatomical properties of the trabecular meshwork are required in order to be able to develop a quantitative predictive model of LT.

## 6. ACKNOWLEDGMENTS

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